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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/041,975	03/13/1998	MARC ALIZON	2356.0011-06	4167

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EXAMINER
PARKIN, JEFFREY S

ART UNIT	PAPER NUMBER
1648	19

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/041,975	Applicant(s) Alizon et al.
	Examiner Jeffrey S. Parkin, Ph.D.	Art Unit 1648

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 03 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on 27 Jun 2000 .

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 23-38 is/are pending in the application.

4a) Of the above, claim(s) 26-38 is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 23-25 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Detailed Office Action

Status of the Claims

1. Applicants' representative requested that the finality of the rejection in the last Office action be withdrawn in a telephonic interview conducted on 20 March, 2002. Applicants noted that a preliminary reply containing remarks and a declaration was filed with the Office on 27 June, 2000. Prior to processing and entry of this reply, a final Office action was mailed on 06 July, 2000. The response of 27 June, 2000, was then improperly entered as an amendment-after-final and an advisory action mailed on 04 December, 2001. In response to applicants' request, the advisory action is hereby vacated and the finality of the Office action mailed 06 July, 2000, is hereby withdrawn. Applicants are again reminded of the restriction requirement set forth in Paper No. 7. Since this application is a CPA filed pursuant to 37 C.F.R. § 1.53(d) based upon parent Application No. 09/041,975 and does not contain an indication that a shift in election is desired, the election made in the prior application is being carried over (see M.P.E.P. ¶ 201.06(d)). Accordingly, claims 26-38 have been withdrawn from further consideration by the Examiner, pursuant to 37 C.F.R. § 1.142(b), as being drawn to a non-elected invention. Claims 23-25 are currently under examination.

35 U.S.C. § 112, First Paragraph

2. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 23-25 stand rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. *In re Rasmussen*, 650 F.2d 1212, 211 U.S.P.Q. 323 (C.C.P.A. 1981). *In re Wertheim*, 541 F.2d 257, 191 U.S.P.Q. 90 (C.C.P.A. 1976). As previously set forth, the claimed invention is broadly directed toward purified HIV-1 variants that differ genetically in the *gag*, *pol*, and *env* coding regions from three known HIV-1 prototypes (e.g., IIIB, BRU, and ARV-2) by the specified amounts (e.g., 3.4% in Gag, 3.1% in Pol, and 13.0% in Env). Additional limitations simply specify that patient antisera are capable of recognizing the variant Gag, Pol, and Env proteins, as well as, the Gag, Pol, and Env proteins of HIV-1_{MAL}. As such, the claim language encompasses a large genus of genotypically/phenotypically unrelated human immunodeficiency viruses.

Applicants are reminded that the essence of the statutory requirement governing written description is whether one skilled in the art, familiar with the practice of the art at the time of the filing date, could reasonably have found the later claimed invention in the specification as filed. *In re Kaslow*, 707 F.2d 1366, 1375, 217 U.S.P.Q. 1089, 1096 (Fed. Cir. 1983). *In re Wilder*, 736 F.2d 1516, 1520 222 U.S.P.Q. 349, 372 (Fed. Cir. 1984, *cert. denied*, 469 U.S. 1209 (1985). *Texas Instruments, Inc.* v. *International Trade Comm'n*, 871 F.2d 1054, 1063, 10 U.S.P.Q.2d 1257, 1263 (Fed. Cir. 1989). Moreover, the courts have stated that the evaluation of written description is highly fact-specific, and that broadly articulated rules are inappropriate. *In re Wertheim*, 541 F.2d 257, 263, 191 U.S.P.Q. 90, 97 (C.C.P.A. 1976). *In re Driscoll*, 562 F.2d 1245, 1250, 195 U.S.P.Q. 434, 438 (C.C.P.A. 1977). It is also important to remember that the true issue in

question is not whether the specification enables one of ordinary skill in the art to make the later claimed invention, but whether or not the disclosure is sufficiently clear that those skilled in the art will conclude that the applicant made the invention having the specific claim limitations. *Martin* v. *Mayer*, 823 F2d 500, 505, 3 U.S.P.Q.2d 1333, 1337 (Fed. Cir. 1987).

To satisfy the written description requirement, a patent specification must describe the claimed invention in sufficient detail that one skilled in the art can reasonably conclude that the inventor has possession of the claimed invention. See, e.g., *Vas-Cath, Inc.* v. *Mahurkar*, 935 F.2d at 1563, 19 U.S.P.Q.2d at 1116. An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention. *Lockwood* v. *American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 U.S.P.Q.2d 1961, 1966 (Fed. Cir. 1997). The claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence. A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. *Fujikawa* v. *Wattanasin*, 93 F.3d 1559, 1571, 39 U.S.P.Q.2d 1895, 1905 (Fed. Cir. 1996).

As previously set forth, and contrary to applicants' assertions,

the disclosure only describes the molecular cloning and characterization of a single novel HIV-1 isolate, designated LAV-1_{MAL}. For example, the specification clearly states (bridging paragraph, pp. 2 and 3) that "a new virus has been discovered that is responsible for diseases clinically related to AIDS and that can be classified as a LAV-1 virus but that differs genetically from known LAV-1 viruses to a much larger extent than the known LAV-1 viruses differ from each other. The new virus is basically characterized by the cDNA sequence which is shown in Figures 7A to 7I, and this new virus is hereinafter generally referred to as "LAV_{MAL}"." The disclosure provides a restriction map for a molecular clone of HIV-1_{MAL} (see CHARACTERIZATION AND MOLECULE CLONING OF AN AFRICAN ISOLATE, pp. 7 and 8, and Figure 1). The complete nucleotide sequence and deduced amino acid sequence of this clone were ascertained (see Figure 7). The nucleotide sequence and deduced amino acid sequence of this novel isolate were compared to other known HIV-1 isolates (e.g., BRU, ELI, and ARV-2) (see Figures 1B-4 and 6). Based upon this comparison the inventors made three general conclusions. First, it was noted (specification, p. 10) that "the protein sequences of the LAV_{ELI} and LAV_{MAL} are more divergent from LAV_{BRU} that are those of HTLV-3 and ARV-2 (FIG. 4A)". Second, applicants reported that the *env* gene is more variable than the *gag* and *pol* genes. Third, it was reported that the divergence between LAV_{ELI} and LAV_{MAL} was comparable to that between LAV_{BRU} and each of the isolates. Thus, the skilled artisan would reasonably conclude that applicants have identified, cloned, and characterized a novel HIV-1 isolate designated MAL. The skilled artisan would also reasonably conclude that applicants ascertained the genetic relatedness of this particular isolate to other known HIV-1 isolates such as HIV-1 ELI, BRU, and ARV-2. However, the skilled artisan would not reasonably conclude that applicants were in possession of any other HIV-1 variant,

particularly one with the claimed limitations. The disclosure fails to provide any other molecular clones and their attendant nucleotide/amino acid sequences. The disclosure fails to identify the isolation, characterization, and nucleotide sequence of other variant HIV-1 MAL isolates. Thus, the applicants were clearly not in possession of the claimed subject matter at the time of filing and the claim language clearly represents an unwarranted attempt to capture subject matter that was clearly not invented by the applicants.

Applicants submitted a declaration under 37 C.F.R. § 1.132 by Denise Guétard in support of their arguments. This declaration is insufficient to overcome the rejection of the claims as addressed below. Applicants argue that the declaration and specification provide support for the characterization of two HIV-1 isolates designated MAL and ELI. This assertion is erroneous as the declaration simply provides a detailed characterization of a single isolate designated HIV-1_{MAL}. The disclosure fails to provide a detailed accounting of the isolation, characterization, and nucleotide sequence of the second isolate ELI. However, it is noted that applicants state that this virus was the subject of a copending application. However, none of the information pertaining to the characterization and isolation of this isolate was provided in the instant application. Furthermore, even if applicants had disclosed the characterization and cloning of two species of HIV-1, it would still be insufficient to support the broad genus currently being claimed. It has been well-documented that the *Lentivirinae* display considerable genotypic/phenotypic heterogeneity. Thus, even given the complete nucleotide sequence of two isolates in the specification, the skilled artisan could not reasonably predict what the precise nucleotide sequence of any other isolate will be. Thus, it is not readily manifest how the applicants could be in possession of an invention that the skilled artisan can not envisage.

Furthermore, while nucleotide sequence comparisons with known viral isolates were performed, the disclosure fails to provide any evidence suggesting that additional HIV-1 isolates, containing the specific claimed limitations, were isolated and purified. Although vague reference was made to "variants of the new virus" on page three of the specification (first paragraph), the disclosure fails to provide any guidance pertaining to the genotypic and phenotypic properties of any of these purified variants. Moreover, the disclosure is clearly directed toward a novel HIV-1 isolate, designated LAV_{MAL}, as set forth throughout the disclosure (e.g., SUMMARY OF THE INVENTION, pages 2-6; EXPERIMENTAL PROCEDURES, pages 18 and 19; bridging paragraph, pages 22 and 23; etc.). Legal precedence clearly dictates that the disclosure of a single or limited number of species, in combination with generic methods for their isolation, does not provide sufficient written description for the broad genus *per se*. *University of California* v. *Eli Lilly* and *Co.*, 43 U.S.P.Q.2d 1398 (C.A.F.C. 1997). *Fiers* v. *Revel*, 984 F.2d 1164, 1171, 25 U.S.P.Q.2d 1601, 1606 (Fed. Cir. 1993). *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.* 18 U.S.P.Q.2d 1016-1031 (C.A.F.C. 1991). Thus, the skilled artisan would reasonably conclude that while applicants were in possession of a purified HIV-1 isolate designated LAV_{MAL}, they were not in possession of any other HIV-1 variants, particularly those with the claimed genetic differences. Once again, it would appear to the skilled artisan that applicants are simply trying to retroactively claim subject matter which was neither contemplated nor described.

Applicants further argue the amino acid sequences of $HIV\text{-}1_{MAL}$ and $HIV\text{-}1_{ELI}$ were described in Figures 3. Accordingly, they conclude that it is illogical to conclude that they were not in possession of these isolates. The Examiner does not dispute this finding. However, it does not remedy the deficiencies and flaws in the specification and fails to support the broad genus of viruses

currently being claimed. Applicants further contend, along with the declaration of Denise Guétard, that the sequence comparisons set forth in Figures 3 place the claimed genus within the possession of the inventors. Once again, this disclosure fails to adequately support the claimed invention. Figures 3 and 4 illustrate that LAV_{MAL} and LAV_{ELI} display 20.7% and 21.7% genetic unrelatedness, respectively, at the amino acid sequence level in the *env* coding region as compared to isolate LAV_{BRU}. These two viruses respectively display 9.8% and 12.0% genetic unrelatedness in the *gag* coding region and 5.5% and 7.7% unrelatedness in the *pol* coding region. Thus, these comparisons do not even agree with the currently claimed limitations of 3.4%, 3.1%, and 13.0% for the *gag*, *pol*, and *env* coding regions. These numbers were actually derived from an amino acid sequence comparison between LAV_{BRU} and ARV-2, not LAV_{MAL} or LAV_{ELI}. Applicants appear to believe that since the nucleotide sequence of their isolate was compared to other known HIV-1 isolates and genetic differences noted, that they are entitled to subject matter encompassing all other HIV-1 variants with the recited characteristics. This analysis is clearly flawed and wholly unsupported by the disclosure. It simply represents an attempt to capture subject matter which was neither contemplated nor adequately described in the instant application. Thus, there is nothing in the specification, declaration, or applicants' arguments that would lead the skilled artisan to conclude that applicants were in possession of the claimed invention at the time of filing.

Moreover, legal precedence also clearly dictates that conception of a chemical compound (e.g., a DNA molecule) is not achieved until reduction to practice has occurred (*University of California* v. *Eli Lilly*, 119 F.3d 1559, 43 U.S.P.Q.2d 1398 (Fed. Cir. 1997); *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 U.S.P.Q.2d 1016-1031 (C.A.F.C. 1991); *Fiers v. Sugano*, 25 U.S.P.Q.2d 1601-1607 (C.A.F.C.

1993); *In re Bell*, 26 U.S.P.Q.2d 1529-1532 (C.A.F.C. 1993); *In re Deuel*, 34 U.S.P.Q.2d 1210-1216 (C.A.F.C. 1995)). In *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.* the court concluded that "It is not sufficient to define it solely by its principal biological property, e.g., encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property. We hold that when an inventor is unable to envision the detailed constitution of a gene so as to distinguish it from other materials, as well as a method for obtaining it, conception has not been achieved until reduction to practice has occurred, i.e., until after the gene has been isolated." The significance of conception and reduction to practice was further addressed by the court in *Fiers v. Sugano* where it was emphasized that "Conception is a question of law, reviewed *de novo* on appeal, and if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated; thus, regardless of complexity or simplicity of method of isolation employed, conception of DNA sequence, like conception of any chemical substance, requires definition of that substance other than by its functional utility." Thus, the courts have emphasized that the inventor must clearly and unambiguously identify the salient characteristics and properties of any given claimed nucleotide sequence. However, the disclosure fails to lead the skilled artisan to any given viral variant. Accordingly, when all the aforementioned factors are considered *in toto*, one of ordinary skill in the art would reasonably conclude that applicants were not in possession of the claimed invention at the time of filing.

35 U.S.C. § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

35 U.S.C. § 103(a)

5. The following is a quotation of 35 U.S.C. § 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103(a).

7. Claims 23-25 stand rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Myers *et al.* (1990). Applicants' contend that the claims are fully supported by the disclosure and are entitled to the benefit of priority to earlier filed U.S. and French applications. As previously set forth, and contrary to applicants' assertion, this application clearly fails to provide an adequate written description of the claimed invention and priority cannot be extended under 35 U.S.C. § 119 or 120. Accordingly, the following art rejection is proper and hereby maintained. Myers *et al.* (1990) provide the complete nucleotide sequence of a novel purified HIV-1 isolate designated Z2Z6. This isolate is genetically related to the HIV-1 isolates ELI and MAL and appears to be only distantly related to the isolates BRU, IIIB (or HXB2), and ARV-2 (SF-2). Nucleotide sequence and amino acid analysis demonstrated that this isolate appears to vary from the aforementioned prototypical isolates BRU, IIIB, and ARV-2 by at least 3.4%, 3.1%, and 13.0% in the *gag*, *pol*, and *env* coding regions, respectively. Thus, this isolate appears to meet all the limitations of the claimed invention. Moreover, because of the close genetic relatedness between Z2Z6 and the isolates ELI and MAL, one of ordinary skill in the art would reasonably expect nucleic acid probes and antibodies specific for MAL to also recognize Z2Z6 nucleic acids and antigens.

Finality of Office Action

8. All claims are drawn to the same invention claimed in the parent application prior to the filing of this Continued Prosecution Application under 37 C.F.R. § 1.53(d) and could have been finally rejected on the grounds of art and record in the next Office action. Accordingly, **THIS ACTION IS MADE FINAL**, even though it is a first action after the filing under 37 C.F.R. § 1.53(d). Applicant is reminded of the extension of time policy as set forth

in 37 C.F.R. § 1.136(a). **A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.**

Correspondence

9. Correspondence related to this application may be submitted to Group 1600 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Official communications should be directed toward one of the following Group 1600 fax numbers: (703) 308-4242 or (703) 305-3014. Informal communications may be submitted directly to the Examiner through the following fax number: (703) 308-4426. Applicants are encouraged to notify the Examiner prior to the submission of such documents to facilitate their expeditious processing and entry.

10. Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (703) 308-2227. The examiner can normally be reached Monday through Thursday from 8:30 AM to 6:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisors, James Housel or Laurie Scheiner, can be reached at (703) 308-4027 or (703) 308-1122, respectively. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 receptionist whose telephone number is (703) 308-0196.

Respectfully,

Jeffrey S. Parkin, Ph.D.
Patent Examiner
Art Unit 1648

JAMES HOUSEL 7/15/02
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

29 June, 2002